General

Guideline Title

Radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan 27. 65 p. (Technology appraisal guidance; no. 376).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- August 31, 2016 – Opioid pain and cough medicines combined with benzodiazepines : A U.S. Food and Drug Administration (FDA) review has found that the growing combined used of opioid medicines with benzodiazepines or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths. FDA is adding Boxed Warnings to the drug labeling of prescription opioid pain and prescription opioid cough medicines and benzodiazepines.
- March 22, 2016 – Opioid pain medicines : The U.S. Food and Drug Administration (FDA) is warning about several safety issues with the entire class of opioid pain medicines. These safety risks are potentially harmful interactions with numerous other medications, problems with the adrenal glands, and decreased sex hormone levels. They are requiring changes to the labels of all opioid drugs to warn about these risks.

Recommendations

Major Recommendations

Radium-223 dichloride is recommended as an option for treating adults with hormone-relapsed prostate cancer, symptomatic bone metastases and

no known visceral metastases, only if:

- They have had treatment with docetaxel, and
- The company provides radium-223 dichloride with the discount agreed in the patient access scheme

People whose treatment with radium-223 dichloride is not recommended in this National Institute for Health and Care Excellence (NICE) guidance, but were started within the National Health Service (NHS) before this guidance was published, should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Hormone-relapsed prostate cancer with bone metastases

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Nuclear Medicine

Oncology

Urology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To assess the clinical effectiveness and cost-effectiveness of radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases

Target Population

Adults with hormone-relapsed prostate cancer, symptomatic bone metastases and no known visceral metastases

Interventions and Practices Considered

Radium-223 dichloride

Major Outcomes Considered

- Clinical effectiveness
  - Overall survival
  - Time to first skeletal-related event
  - Incidence of individual skeletal-related events
  - Changes and time to prostate-specific antigen (PSA) progression
  - Changes and time to progression in total alkaline phosphatase (ALP) and change in bone ALP
  - Pain
  - Use of opioid analgesics
  - Health-related quality of life
  - Adverse effects of treatment
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by Aberdeen Health Technology Assessment (HTA) Group (see the "Availability of Companion Documents" field). See the manufacturer's submission (see the "Availability of Companion Documents" field) for details on search strategies.

Clinical Effectiveness

Critique of the Methods of Review(s)

Description of Manufacturer's Search Strategies and Critique

The manufacturer stated that literature searches were undertaken in February 2013 with no date restrictions imposed on the searches. A wide range of databases were searched including conference proceedings from 2008 to 2013 and reference lists of articles were checked as appropriate. Full details of the search strategies were included in the manufacturer's submission (MS).

The searches were designed to identify trials of effectiveness of radium-223 and its comparators but they were not designed to identify studies reporting data relating to adverse events; therefore, it is possible that relevant information may have been missed.

The sources used for the identification of studies were appropriate and the search strategies were comprehensive, although the use of the English language limit and of study design filters in MEDLINE and EMBASE which were designed mainly to identify randomised controlled trials (RCTs) may have resulted in the omission of some relevant studies. Furthermore, while there were no date restrictions imposed on the search, the manufacturer has not stated the date ranges of the databases used. However, the ERG replicated the manufacturer's searches and retrieved similar numbers of results. Controlled vocabularies and free text searching were used effectively and included a wide range of synonyms. The facets of the

search (castration-resistant prostate cancer; radium-223, abiraterone; clinical trials), and the synonyms within each facet, were combined correctly with Boolean operators. Overall, the search strategies were highly sensitive and fit for purpose and the ERG believes that it is unlikely that any relevant studies have been missed.

Eligibility Criteria in the Systematic Review

The eligibility criteria used in the systematic review of clinical effectiveness were given in the MS.

Although one search was conducted, two separate inclusion criteria were applied by the manufacturer for 1) the comparison between radium-223 dichloride and best standard care and 2) the indirect comparison analyses including radium-223, abiraterone and best standard care as potential comparators.

For the network meta-analysis, the manufacturer introduced two further inclusion criteria. To be eligible a study must: 1) use the licensed dosing regimen or the proposed licensed dosing regimen and 2) be available as a full publication (where available). These additional criteria resulted in BC1-02 trial being excluded from the indirect comparison analyses. In their response to the ERG's clarification questions the manufacturer clarified that BC1-02 was dropped from the indirect comparison because only four injections of 50 kilobecquerel (kBq) per kg body weight were administered at four week intervals, whereas the proposed licensed dosing regimen for radium-223 dichloride is six injections of 50 kBq per kg body weight at four week intervals. The manufacturer also clarified that the second restriction did allow the inclusion of conference abstracts if no full publication were available. This meant that the ALSYMPCA study, only available as an abstract at the time of submission, was still eligible for inclusion.

The ERG was concerned that there was no clear rationale for applying two different sets of inclusion criteria so that BC1-02 was eligible for a meta-analysis of radium-223 dichloride versus best standard care but not for a wider network meta-analysis.

Studies Included in the Review

After reasonable exclusions, the MS states that one phase-three RCT and one phase-two RCT of radium-223 dichloride versus placebo plus best supportive care (BSC); two phase-two dose ranging RCTs of radium-223 dichloride; two phase-three RCTs of abiraterone versus placebo plus prednisone and four single-arm studies of abiraterone were considered eligible for inclusion. Figure 2 of the ERG report shows the number of studies included and excluded at each stage of the review.

The manufacturer excluded the two dose-ranging RCTs of radium-223 dichloride. The two RCTs and four single-arms studies of abiraterone were excluded due to the manufacturer's claim that patient heterogeneity precluded any meaningful comparison with the ALSYMPCA trial. The manufacturer's clinical evidence comes from two RCTs of radium-223 dichloride versus placebo plus best supportive care (BSC) (ALSYMPCA and BC1-02).

The ERG believes that it was not appropriate to exclude the abiraterone RCTs from the systematic review. The abiraterone studies clearly met the inclusion criteria for the review.

Cost-effectiveness

ERG Comment on Manufacturer's Review of Cost-effectiveness Evidence

The manufacturer carried out a full systematic review to identify relevant cost-effectiveness studies. The ERG believes that the MS systematic review was of good quality.

The manufacturer states that three different sets of searches were carried out; firstly, to inform the review of cost-effectiveness, secondly, to identify health-related quality of life (HRQL) data in adults with metastatic castration-resistant prostate cancer (mCRPC) and thirdly, to identify HRQL data in adults with bone metastases or who have experienced skeletal-related events (SREs).

All searches were undertaken in February 2013 and were restricted to English language publications between 2000 and 2013. MEDLINE, MEDLINE In-Process, EMBASE, PubMed, EconLIT and National Health Service Economic Evaluation Database (NHS EED) were searched. Full details of the search strategies are included the MS (and are reproducible).

The sources used for the identification of studies were appropriate and the search strategies were comprehensive, with search filters and date and language restrictions used where appropriate.

Inclusion/Exclusion Criteria

For all reviews, the considered patient population included adults with castration-resistant prostate cancer and/or adults with bone metastases and all lines of therapy. All reviews were also restricted to English language publications published since 2000. Details of the remaining inclusion criteria

are presented for each of the reviews in the MS.

Studies Included/Excluded

After reasonable exclusions, nine articles were included in the cost-effectiveness review. Eight of the nine studies were based on Markov models. The remaining study was based on a decision-analytic model.

Conclusion

The manufacturer has not stated any conclusions from the review. The ERG notes that no included studies fully addressed the decision problem in this appraisal.

Number of Source Documents

Clinical Effectiveness

- Twenty-three studies were included in qualitative synthesis.
- Clinical effectiveness of radium-223 dichloride came from two randomised controlled trials (RCTs) (ALSYMPCA and BC1-02).

Cost-effectiveness

- Nine studies were included in the cost-effectiveness review. The Evidence Review Group (ERG) notes that no included studies fully addressed the decision problem in this appraisal.
- The manufacturer submitted an economic model.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by Aberdeen Health Technology Assessment (HTA) Group (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Critique of the Methods of Review(s)

The evidence provided by the manufacturer on the clinical effectiveness of radium-223 dichloride came from two randomised controlled trials (RCTs) (ALSYMPCA and BC1-02).

Approach to Quality Assessment for Included Trials

The manufacturer assessed the quality of the BC1-02 and ALSYMPCA trials. Although it is unclear if a specific quality assessment tool was used, the methods used for quality assessment were considered adequate by the ERG. The methodological quality of the trials was good.

Description and Critique of Methods of Any Meta-analysis

No attempt was made to meta-analyse the results of the two trials due to the different number of administered doses of radium-223 dichloride (six in ALSYMPCA versus four in BC1-02); difference in inclusion criteria for life expectancy (six months in ALSYMPCA versus three months in BC1-02); patients in ALSYMPCA could receive bisphosphonates as part of best supportive care (BSC), whereas bisphosphonate treatment within three months prior to study entry was an exclusion criteria for BC1-02; and a requirement for external beam radiation therapy (EBRT) was an inclusion criterion for BC1-02 but patients could have been treated with regular analgesia or EBRT for bone pain in the previous 12 weeks in ALSYMPCA. The ERG is satisfied that the difference in dosing administration renders the intervention sufficiently different that clinical heterogeneity precludes statistical pooling of results. The ERG also notes that the BC1-02 trial is a much smaller trial in comparison to ALSYMPCA.

Description and Critique of Methods of Any Indirect Comparison

Three studies (ALSYMPCA, COU-AA-301 and COU-AA-302) were eligible for inclusion in a possible indirect comparison (network meta-analysis). This would involve a network of three treatments: radium-223 dichloride, abiraterone and best standard care/placebo. However, the manufacturer decided not to conduct such an analysis.

The manufacturer justifies the reason for not performing meta-analyses in either setting by stating that other trials are not similar to ALSYMPCA. These differences include the fact that prednisone was taken by all patients in the abiraterone studies, differences in allowable concomitant medication, differences in rates of bone metastases and European Cooperative Oncology Group (ECOG) performance status and differences in study outcome measures.

The ERG believes that in principle a network meta-analysis would have been possible for some outcomes such as overall survival, but the ERG accepts that the populations who have and have not received prior docetaxel are distinct patient groups and agrees that it may not be sensible to combine these studies in a network-meta-analysis. It would have been possible to split ALSYMPCA into two subgroups based on prior docetaxel status and include in separate analyses with the abiraterone studies, although the benefits of a randomised design would be lost and they would have had to be treated as observational studies.

See Section 4 of the ERG report (see the "Availability of Companion Documents" field) for additional information on clinical effectiveness analysis.

Cost-effectiveness

Summary and Critique of Manufacturer's Submitted Economic Evaluation by the ERG

Model Structure

The manufacturer develops a *de novo* model of the cost effectiveness of radium-223 compared to best supportive care, or placebo. It is a cost-utility model with a weekly cycle and a five-year time horizon. The model estimates the overall survival in each arm up to the end of the five-year time horizon. For each cycle, the remaining survivors are divided into those:

- Without progression and without an on study skeletal-related event (SRE)
- With progression and without an on study SRE
- Without progression and with an on study SRE
- With progression and with an on study SRE

Adverse events are included within the modelling, with health-related quality of life and cost allowances for these being added to the first cycle of the model.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Consideration

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Care Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the Appraisal Consultation Document (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE Web site. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the Final Appraisal Determination (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Summary of Appraisal Committee's Key Conclusions

Availability and Nature of Evidence

Given that the company did not submit evidence comparing radium-223 with docetaxel, the Committee could only consider the cost effectiveness of radium-223 compared with best supportive care for people in whom docetaxel is contraindicated or unsuitable, and for radium-223 compared with abiraterone in people who have previously had docetaxel.

Uncertainties Around and Plausibility of Assumptions and Inputs in the Economic Model

The Committee concluded that the company's choice of a 5-year time horizon was not in line with the National Institute for Health and Care Excellence (NICE) reference case and that a lifetime time horizon would have been more appropriate to capture all relevant costs and benefits. The Committee accepted prostate specific antigen (PSA) progression for the comparison with abiraterone in the absence of any other alternative measure of progression, but for the comparison with best supportive care, it considered that alkaline phosphatase (ALP) progression was the most appropriate measure of progression on which to base its decision.

The Committee noted that only 1 person was at risk of death after 3 years, and it considered that doubling the weekly probability of mortality at a time-point when more people were at risk would be more informative. The Committee further concluded that in general, there was uncertainty in the company's approach of modelling overall survival, including the choice of parametric distribution used.

The Committee agreed that the calculation of the cohort flow was an important issue and there was uncertainty relating to the most appropriate approach.

The Committee concluded that although the quality-of-life benefits with radium-223 compared with best supportive care could extend beyond 24 weeks, the duration of this benefit is uncertain, but would likely diminish over time and could not be assumed to extend over a person's lifetime.

The Committee noted that there was added uncertainty in the assumptions about waste, which had not been accounted for either radium-223 or abiraterone. It agreed that the true costs of treatment waste were difficult to estimate but concluded that incorporating waste into the comparison of radium-223 with best supportive care would worsen the cost-effectiveness estimates for that comparison.

The Committee had not received any data or information that would help quantify any additional costs and so it concluded that the potential additional cost to the National Health Service (NHS) of providing treatment with radium-223 was uncertain.

The Committee noted that the company had assumed, in addition to routine follow-up visits, an additional £161 monthly administration cost for abiraterone, and that it had calculated the cost of abiraterone based on calendar months rather than 4 weeks. It concluded that the company's estimated costs for abiraterone may have been overestimated.

Incorporation of Health-related Quality-of-Life Benefits and Utility Values. Have Any Potential Significant and Substantial Health-related Benefits Been Identified That Were Not Included in the Economic Model, and How Have They Been Considered?

The Committee considered that fatigue was already captured in the quality-adjusted life year (QALY) calculation through the other dimensions of the EuroQuol 5-dimension (EQ-5D), and that there were no additional gains in health-related quality of life over those already included in the QALY calculations. Therefore, the Committee concluded that the innovative aspects of radium-223 were already incorporated in the economic analyses.

Are There Specific Groups of People for Whom the Technology Is Particularly Cost Effective?

None

What Are the Key Drivers of Cost-effectiveness?

For the comparison with abiraterone, there were marginal differences in QALYs, which meant small differences in costs had a large effect on the results.

For the comparison of radium-223 with best supportive care, the assumptions around the modelling of survival, calculation of the cohort flow and the duration of quality-of-life benefits were the key drivers of the cost-effectiveness results.

Most Likely Cost-effectiveness Estimate (Given as an Incremental Cost-effectiveness Ratio [ICER])

The Committee concluded that the most plausible ICER for radium-223 compared with best supportive care for those people who have not had prior docetaxel, and for whom docetaxel is contraindicated or unsuitable was likely to be above £50,000 per QALY gained.

The Committee was unable to make any recommendations for radium-223 for people who can have docetaxel because no evidence was submitted by the company.

The Committee took a pragmatic approach of judging uncertainties based on multiple factors and concluded that the most plausible ICER for radium-223 compared with abiraterone would fall within the acceptable range.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination (FAD).

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups

- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Appraisal Committee considered evidence submitted by the company that holds the marketing authorisation for radium-223 and a review of this submission by the Evidence Review Group (ERG). The key clinical evidence in the company's submission came from ALSYMPCA, the pivotal phase-III trial. For cost-effectiveness, the Appraisal Committee considered an economic model submitted by the manufacturer.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases resulting in delayed disease progression and prolonged survival

Potential Harms

The summary of product characteristics lists the following adverse reactions for radium-223: thrombocytopenia, diarrhoea, vomiting, nausea, neutropenia, pancytopenia, leukopenia, injection-site reactions and lymphopenia.

For full details of adverse reactions and contraindications, see the summary of product characteristics.

Contraindications

Contraindications

For full details of contraindications, see the summary of product characteristics.

Qualifying Statements

Qualifying Statements

- The recommendations in this guidance represent the view of the National Institute for Health and Care Excellence (NICE), arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance are at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.
- Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the National Health Service (NHS) Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce

health inequalities.

Implementation of the Guideline

Description of Implementation Strategy

- Section 7(6) of the National Institute for Health and Care Excellence (NICE) (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, National Health Services (NHS) England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.
- The Welsh Assembly Minister for Health and Social Services has issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 3 months of the guidance being published.
- When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has hormone-relapsed prostate cancer, symptomatic bone metastases, no known visceral metastases and only if they have had treatment with docetaxel and the doctor responsible for their care thinks that radium-223 is the right treatment, it should be available for use, in line with NICE's recommendations.
- The Department of Health and Bayer have agreed that radium-223 will be available to the NHS with a patient access scheme which makes it available with a discount. The size of the discount is commercial in confidence. It is the responsibility of the company to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about the patient access scheme should be directed to Lesley Gilmour (lesley.gilmour@bayer.com).

Implementation Tools

Foreign Language Translations

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan 27. 65 p. (Technology appraisal guidance; no. 376).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Jan 27

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Appraisal Committee

Composition of Group That Authored the Guideline

Committee Members: Professor Gary McVeigh (*Chair*), Professor of Cardiovascular Medicine, Queen's University Belfast and Consultant Physician, Belfast City Hospital; Dr Lindsay Smith (*Vice Chair*), GP, West Coker Surgery, Somerset; Dr Aomesh Bhatt, Regulatory and Medical Affairs Director Europe and North America, Reckitt Benckiser; Dr Andrew Black, GP, Mortimer Medical Practice, Herefordshire; Professor David Bowen, Consultant Haematologist, Leeds Teaching Hospitals NHS Trust; Dr Matthew Bradley, Therapy Area Leader, Global Health Outcomes, GlaxoSmithKline; Dr Ian Campbell, Honorary Consultant Physician, Llandough Hospital, Cardiff; Ms Tracey Cole, Lay Member; Dr Ian Davidson, Lecturer in Rehabilitation, University of Manchester; Mr John Dervan, Lay Member; Professor Simon Dixon, Professor of Health Economics, University of Sheffield; Dr Martin Duerden, Assistant Medical Director, Betsi Cadwaladr University Health Board, North Wales; Mrs Susan Dutton, Senior Medical Statistician, Oxford Clinical Trials Research Unit; Mr Christopher Earl, Surgical Care Practitioner, Wessex Neurological Centre at University Hospital Southampton NHS Foundation Trust; Mrs Gillian Ells, Prescribing Advisor – Commissioning, NHS Hastings and Rother and NHS East Sussex Downs and Weald; Professor Paula Ghaneh, Professor and Honorary Consultant Surgeon, University of Liverpool; Dr Susan Griffin, Research Fellow, Centre for Health Economics, University of York; Professor Carol Haigh, Professor in Nursing, Manchester Metropolitan University; Professor John Henderson, Professor of Paediatric Respiratory Medicine, University of Bristol and Bristol Royal Hospital for Children; Dr Paul Hepple, GP, Muirhouse Medical Group; Professor John Hutton, Professor of Health Economics, University of York; Professor Peter Jones, Emeritus Professor of Statistics, Keele University; Professor Steven Julious, Professor in Medical Statistics, University of Sheffield; Dr Tim Kinnaird, Lead Interventional Cardiologist, University Hospital of Wales, Cardiff; Dr Warren Linley, Independent Pharmacist and Health Economist; Dr Malcolm Oswald, Lay Member; Professor Femi Oyebode, Professor of Psychiatry and Consultant Psychiatrist, The National Centre for Mental Health; Dr Paul Parvulescu, Consultant in Public Health Medicine, Liverpool County Council; Dr John Radford, Director of Public Health, Rotherham Primary Care Trust and Metropolitan Borough Council; Dr Mohit Sharma, Consultant in Public Health, Public Health England; Dr Brian Shine, Consultant Chemical Pathologist, John Radcliffe Hospital, Oxford; Dr Murray Smith, Associate Professor in Social Research in Medicines and Health, University of Nottingham; Mr Paddy Storrie, Lay Member; Dr Alison Talbot-Smith, Consultant in Public Health, Herefordshire Clinical Commissioning Group

Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in ePub and eBook formats from the NICE Web site .

Availability of Companion Documents

The following are available:

- Radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases. Costing report. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan. 3 p. (Technology appraisal guidance; no. 376). Available from the National Institute for Health and Care Excellence (NICE) Web site .
- Robertson C, Lam T, Stewart F, Scott NW, Cummins E, Ramsay CR. Radium-223 for the treatment of bone metastases in hormone relapsed prostate cancer. Aberdeen (UK): Aberdeen HTA Group; 2013 Aug. 122 p. Available from the NICE Web site .
- Radium-223 dichloride solution for injection for the treatment of castration-resistant prostate cancer with bone metastases. Single technology appraisal. Manufacturer's submission. Bayer; 2013 Jun. 384 p. Available from the NICE Web site .

Patient Resources

The following is available:

- Radium-223 dichloride for treating hormone-relapsed prostate cancer with bone metastases. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Jan. 3 p. (Technology appraisal guidance; no. 376). Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in ePub and eBook formats from the NICE Web site . Also available in Welsh from the NICE Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on April 14, 2016. This summary was updated by ECRI Institute on October 21, 2016 following the U.S. Food and Drug Administration advisory on opioid pain and cough medicines combined with benzodiazepines.

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